REMARKS

Claims 1-9 are pending and under examination. New claims 39-47 have been added. Support for the new claims can be found throughout the specification and the claims as filed. In particular, support for the new claims can be found in original claims 1-9 and on page 8, line 26, to page 9, line 5. Accordingly, these new claims do not raise an issue of new matter, and entry thereof is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 1-9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants respectfully maintain that the specification provides sufficient description and guidance to convey to one skilled in the art that Applicants were in possession of the claimed methods at the time the application was filed.

In the Office Action on page 3, it is asserted that claims 6 and 7 require specific techniques of producing the ligands with recombinant expression in melanophore cells. Applicants point out that claims 6 and 7 recite recombinant expression of the receptor variant population, not producing the ligands recombinantly. Furthermore, the specification provides teachings of well known methods of recombinant expression in cells, and in particular, melanophore cells (see page 25, lines 8-32, and Example I, pages 37-40). For example, the specification teaches specific procedures for deriving melanophore cells (page 37, line 15, to page 38, line 5) and transfecting DNA constructs into melanophore cells (page 39, lines 1-10). Furthermore, producing receptors by recombinant expression in melanophore cells was well known in the art and is described, for example, by Lerner et al. in U.S. Patent No. 5,462,856, which was cited by the Examiner and provided in the previous response as Exhibit A (see, for example, column 13, line 18, to column 14, line 67). Therefore, based on the teachings in the specification and what was well known in the art, one skilled in the art would readily understand that the specification provides sufficient description and guidance for expressing receptor variants in cells, including melanophore cells.

In regard to tagging ligands, the specification teaches methods of tagging variants (page 28, line 28, to page 30, line 24). For example, the specification teaches that a large number of tags can be generated with a limited number of different peptides and antibodies specific for those peptides (page 29, line 30, to page 30, line 4). In addition, the specification gives an example of the use of 32 different peptides to generate 4096 different tags (page 30, lines 1-4). Furthermore, the specification teaches methods for detecting the tag, for example, using antibodies specific for the peptides in FACS analysis (page30, lines 8-20). Moreover, the specification provides an example, Example I, where a variant receptor population is tagged by co-expression of a peptide tag on the parental expression vector (page 38, lines 18-33).

Furthermore, the specification exemplifies the claimed methods using a receptor variant population in Examples II-V. In the Office Action, it is asserted that Example V describes antibody ligands to BR96 antibody receptor variants but is not commensurate in scope with the claims. Example V exemplifies the claimed method for determining binding of a receptor to one or more ligands by contacting a collective receptor variant population with one or more ligands and detecting binding of the one or more ligands to the collective receptor variant population Therefore, Applicants respectfully maintain that the specification provides sufficient description and guidance for the claimed methods.

The Office Action indicates on page 5, paragraph 8, that adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that compounds falling within the scope possess utility and demonstrate that Applicant was in possession of the claimed invention. The Office Action further asserts that "[T]he more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure." Applicant's representative is not aware of the precedent for such an assertion with respect to written description and would appreciate being provided with the relevant authority so that the case law can be reviewed and responded to appropriately.

Applicants respectfully maintain that one skilled in the art, based on the teachings in the specification and what was well known to those skilled in the art, would understand that the

specification provides sufficient description for the claimed methods. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 1 and 9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicants respectfully maintain that the specification provides sufficient description and guidance to enable the claimed methods.

Regarding the alleged breadth of the claims, the specification teaches properties of a receptor and ligand, for example, that a receptor selectively binds to a ligand (page 5, lines 28, to page 6, line 17). In addition, the specification provides sufficient description and examples of various types of receptors and ligands (see, for example, page 6, lines 11-17; page 7, lines 4-16; and page 17, line 5, to page 18, line 27). Furthermore, a specific working example of receptors and ligands is shown in Example V, where the BR96 antibody is designated as a parent receptor and anti-idiotypic antibodies are ligands (page 49, lines 8-9, and page 50, lines 29-33). Thus, based on the teachings in the specification, one skilled in the art would have readily understood that the claimed receptors and ligands are binding partners having specific binding activity.

Regarding the alleged unpredictability in the art, Applicants respectfully submit that the specification provides sufficient description and guidance to enable the invention as claimed. The Office Action acknowledges that ligand/receptor binding pairs were well-known in the art at the time of the invention but alleges that only limited numbers of such pairs were known. As discussed in the previous response, Applicants maintain that a number of ligand/receptor binding pairs were known in the art at the time of filing of the application, thus contributing to predictability in the art. In the previous response, evidence in the form of various publications describing ligand/receptor pairs was provided. These publications demonstrate that a number of ligand/receptors binding pairs with diverse structures were known in the art at the time of filing of the application.

In the Office Action on page 12, it is indicated that Applicants pointed out in the last response various ligand/receptor pairs taught by the prior art, but the Office Action indicates that the "claims are not limited to such pairs or even to *any* specific pair." Applicants respectfully

point out that, in the previous response, Applicants were addressing the assertion by the Examiner that "only limited numbers of such [ligand/receptor] pairs were known." Applicants provided in the previous response evidence of exemplary ligand/receptor pairs to establish what was well known to those skilled in the art, that in fact hundreds to thousands of ligand-receptor pairs were known in the art at the time of filing of the application, not "only limited numbers of such pairs" as asserted in the previous Office Action. Furthermore, the claims are directed to methods of determining binding of a receptor to one or more ligands. To limit the claims to a receptor-ligand pair, and certainly to "*any* specific pair" would unduly narrow the claim since the purpose of the claim is to determine binding of a receptor to one or more ligands. Limitation to a specific ligand/receptor pair would require that the result of the method claim already be known before the method is performed.

Regarding the alleged unpredictability of adding tags to ligands, the Office Action cites an article by Janda (Proc. Natl. Acad. Sci. USA 91:10779-10785 (1994)) as describing the unpredictability of tagging methods. However, as discussed in the previous response, the article by Janda cites several references that have successfully used different tagging methods. These methods include diverse tagging strategies such as phage display, a "peptides on plasmids" method by Affymax, a peptide coded library method by Chiron Corporation, electrophoric tagging, and encoded combinatorial libraries. Thus, Janda supports the teachings in the specification that one skilled in the art would expect to successfully tag a ligand variant population without undue experimentation.

The Office Action alleges that the specification provides no specific examples of the claimed methods where the receptors are tagged. In regard to tagging ligands, the specification teaches methods of tagging variants (page 28, line 28, through page 30, lines 24). Methods for detecting the tag, for example using antibodies specific for the peptides in FACS analysis, are also described (page 30, lines 8-20). The specification also teaches methods for tagging a variant by co-expression of a peptide tag on the parental expression vector (Example I on page 38, lines 18-33). Therefore, Applicants respectfully submit that the specification provides sufficient description for how to tag a variant and identify the tag.

Applicants respectfully maintain that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claim 5 under 35 U.S.C. § 112, second paragraph, is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that the phrase "optimal binding activity" is clear and definite. Nevertheless, claim 5 has been amended to recite that the receptor variant has optimal binding activity to one or more ligands "relative to a parent receptor of the receptor variant population." Applicants respectfully submit that claim 5 is clear and definite and, accordingly, respecfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1-8 under 35 U.S.C. § 102(b) as allegedly anticipated by Lerner et al., U.S. Patent No. 5,462,856, is respectfully traversed. Applicants maintain that the claimed methods are novel over Lerner et al.

As discussed in the previous response, Applicants respectfully maintain that the claims are novel over Lerner et al. At best, Lerner et al. merely describes the cloning of GPCRs in the melanophore system using random cDNA libraries. In contrast, the subject specification teaches the use of a collective receptor variant population and not random cDNA libraries. For example, the specification describes variations of a parent receptor that can make up a collective receptor variant population (see, for example, page 8, line 26, to page 9, line 25). Thus, the Lerner et al. reference does not teach each element of the claimed invention and, therefore, it cannot anticipate the claimed invention. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

Respectfully submitted,

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Deborah L. Cadena
Registration No. 44,048
Telephone: (858) 535-9001
Facsimile: (858) 535-8949

McDERMOTT, WILL & EMERY
4370 La Jolla Village Drive
7th Floor
San Diego, California 92122